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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/524,486      | 11/17/2005  | Stefan Laufer        | 264821US0PCT        | 6298             |

22850 7590 12/11/2007  
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.  
1940 DUKE STREET  
ALEXANDRIA, VA 22314

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| EXAMINER |
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MORRIS, PATRICIA L

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1625

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| NOTIFICATION DATE | DELIVERY MODE |
|-------------------|---------------|

12/11/2007

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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## Office Action Summary

**Application No.**

10/524,486

**Applicant(s)**

LAUFER ET AL.

**Examiner**

Patricia L. Morris

**Art Unit**

1625

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 October 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 16-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Claims 16-37 are under consideration in this application.

#### *Election/Restrictions*

The restriction requirement is deemed sound and proper and is hereby made FINAL.

Again, This application has been examined to the extent readable on the elected compound wherein R<sup>10</sup> represents a tetrahydropyran and nonheterocyclic groups, B represents nonheterocyclic groups and R<sup>1</sup>-R<sup>7</sup>, A, m and n as set forth in claim 25, exclusively. Claims 24 and 34 have been examined to the extent readable on the treatment of rheumatoid arthritis since applicants have failed to submit an **independent** claim directed solely to the elected method, *i.e.*, the treatment of rheumatoid arthritis.

#### *Claim Rejections - 35 USC § 102*

The rejection of claims 16-37 under 35 USC 102 is hereby withdrawn in view of applicants' submission of a certified english translation of their priority document.

#### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 16-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Laufer et al. for the reasons set forth in the previous Office action.

The reference of Beers et al. has been withdrawn in view of applicants' assertions in the instant response.

Again, Laufer et al. generically embrace the instant compounds. Note the compounds of formula (I) wherein Ar is (optionally substituted) phenyl, het is (optionally substituted) 4-pyridine and A is an alkylene chain in claim 1 of Laufer et al.

Applicants appear to argue that one having ordinary skill in the art would not have been motivated to produce the compounds encompassed by the claims. The motivation is not abstract but is always related to the properties or uses that one having ordinary skill in the art would have expected the resulting compound to exhibit. In situations involving chemical compounds bearing a close structural similarity, the requisite motivation stems from the expectation that compounds exhibiting closely similar structures will exhibit similar properties. In the situation here, one would not have to modify the disclosure of Laufer et al., but merely employ compounds that are generically embraced in a narrow manner by the disclosed formula of As previously discussed, the requisite motivation for producing the claimed compounds stems from the fact that they are generically disclosed.

The declaration of Albrecht, filed on October 1, 2007, while interesting, if of little if any probative value because it is not commensurate in scope with the claims and fails to include

the closest prior art compounds, *i.e.*, wherein R<sup>10</sup> represents –A-phenyl (optionally substituted) and the **elected** compound of example 54.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 34, 36 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Contra to applicants’ assertions in the instant response, applicants have failed to present any objective evidence that the claimed compounds treat rheumatoid arthritis. Applicants merely assert that the examiner has not convincingly indicated why the compounds are not enabled.

This is clearly not persuasive. Applicants were given several references as to why the specification in non-enabling.

***The nature of the invention***

The nature of the invention is drawn to the method of using the instant compounds in the treatment of rheumatoid arthritis in which inhibition of release of a cytokine is required.

***State of the Prior Art and the level of skill in the art***

It is well recognized in the art that there is only a limited understanding of the activities of several cytokines as they relate to their particular biological functions. Odeh (Clinical Immunology and Immunopathology, 83, pp. 103-116, 1997) on page 103 recite that current treatments of rheumatoid arthritis are inadequate. The art recognizes that specific antirheumatic drugs do not inhibit all cytokines and the mechanisms of action are unclear. See Bondenson, Gen. Pharmac., 29, pp127-150, 1997).

***Predictability/unpredictability of the art.***

The high degree of unpredictability is well recognized in cytokine inhibition. Rheumatoid arthritis has always been one of the most difficult autoimmune disease to understand and treat. Campbell et al. (Immunology and Cell Biology, 2003, 81, pages 354-366) on page 362, states that a TNF-driven cytokine hierarchy seems untenable, in view of the fact that some TNF inhibitors have some but not all clinical benefits in patients. The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seeming high level of skill in the art. The existence of these obstacles established that the contemporary

knowledge in the art would prevent one of ordinary skill in the art from accepting any treatment regimen on its face.

***The amount of direction or guidance and the presence or absence of working examples***

The specification is silent as to whether if any compound treats rheumatoid arthritis.

***The breadth of the claims***

The breadth of the claims are drawn to the treatment of rheumatid arthritis.

***The quantity of experimentation needed***

In view of high degree of unpredictability in the art, the limited working example with no results and the fact that the breadth of the claims is not commensurate with that of any objective enablement and that the nexus between inhibition of cytokine release and rheumatoid arthritis has not been established, the quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the compounds and pharmaceutical compositions.

The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. Applicants are referred to In re Fouche, 169 USPQ 429 CCPA 1971, MPEP 716.02(b). Applicants are also referred to In re Wands, 858 f.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in Ex parte Foreman, 230 USPQ 546 (Bd. Of App. and Inter 1986).

In terms of the 8 Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of unpredictability in the art of the invention, and the poor amount of direction provided by

applicants. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 10, 13 and 14 of U.S. Patent No. 6,432,988.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant compounds are disclosed therein.



Applicants have failed to file a terminal disclaimer.

Claims 16-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-17 of copending Application No. 10/514,911. Although the conflicting claims are not identical, they are not patentably distinct from each other because for the reasons set forth in the previous Office action.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The claims in the instant application are not allowable and hence, this above rejection is maintained.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

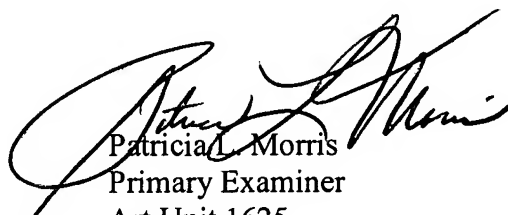
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia L. Morris whose telephone number is (571) 272-0688. The examiner can normally be reached on Mondays through Fridays.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Patricia L. Morris  
Primary Examiner  
Art Unit 1625

plm  
December 5, 2007